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EXAMINER	
HA, JULIE	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,323	EBRIGHT, RICHARD H	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-101 and 103-120* is/are pending in the application.

4a) Of the above claim(s) *78-83 and 104-120* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84-90,92-101 and 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-Final rejection filed on June 15, 2007 is acknowledged. Claims 91 and 102 have been cancelled. Claims 78-101 and 103-120 are pending in this application.

Applicant elected with traverse of Group II (claims 84-103) on December 04, 2006. Restriction and species election requirements were deemed proper and made FINAL in the previous office action. Claims 78-83 and 104-120 are withdrawn from consideration as being drawn to a non-elected invention. Claims 84-90, 92-101 and 103 are examined on the merits in this office action.

Julie Ha is the Examiner of record.

Maintained Rejections

35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 84-90, 92-101 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delgado et al (Journal of Bacteriology, 2001, 183: 4543-4550) in view of Korzheva et al (Science, 2000, 289: 619-625), Darst et al (PG Pub 2002/0034808) and Woychik (Cell, Feb 2002, 108: 453-463).

4. The instant claims are drawn to method of identifying an agent that inhibits RNA synthesis activity of E. coli RNAP by binding to an RNAP secondary channel amino acid sequence. The claims are further drawn to comparing the inhibition by an agent that binds to the secondary channel with inhibition by an agent that binds to a mutant channel or one that binds to fragment of RNAP.

5. With respect to claims 84-89 and 93-100, Delgado et al disclose methods to identify an agent that binds to the secondary channel by determining the binding site of the antibiotic MccJ25 within the intact E. coli RNAP. Delgado et al further disclose that such methods involve contacting the RNAP with the antibiotic and detecting the inhibition of RNA synthesis in presence of MccJ25 via a transcription assays (see kinetics of biding, Materials and Methods). Delgado et al also disclose a mutant residing in the homology block G of the b' subunit (see abstract) of RNAP and comparative methods employing such a mutant in presence of the antibiotic versus the intact polymerase in presence of the antibiotic to identify the presence or absence of binding. Resistance to the antibiotic was indicative of the antibiotics ability to bind to RNAP in the absence of mutation. Delgado et al disclose that the affected mutation is conserved in all prokaryotic homologues examined (Figure 2), which is good evidence to indicate that

the region that contains the mutation is part of the catalytic center of the enzyme, and that which is responsible for the transcription properties of RNAP. The difference between the reference and the instant claims is that the reference does not explicitly recite binding of the agent to the RNAP secondary channel.

6. However, Korzheva disclose a model based on a bacterial x-ray crystal structure (p. 620, first paragraph) known in the art wherein the secondary channel is responsible for the diffusion of incoming nucleotide substrates into the active site (Figure 3) to overcome access to the main channel which is blocked by the nucleic acid framework.

7. Therefore, it would have been obvious to one of ordinary skill in the art to use the method of identifying an agent that binds to a specific domain of RNAP to inhibit RNA synthesis, and to combine the method with agents with potential to bind to the secondary channel as modeled by Korzheva for the known and expected result of providing a means recognized in the art to identify regions in RNAP that contribute to sensitivity towards agents with inhibition of RNA synthesis activity for the development of a new antibiotic.

Response to Applicant's Arguments

8. Applicant argues that the claims are directed to methods of identifying an agent that binds to and/inhibits a bacterial RNAP homologous secondary channel amino acid sequence, and the amended claims not recite that the bacterial RNAP homologous secondary channel amino acid sequence corresponds to, and is alignable with amino acid residues 736-747 and 779-781 or the β' subunit of RNAP from *E. coli*. Furthermore,

Applicants argue that the claims are further directed to comparing the inhibition by an agent that binds to this specific target sequence with inhibition by an agent that binds to a bacterial RNAP derivative that includes at least one substitution, insertion or deletion of amino acid residues in the target region. Further, Applicant argues that Delgado is completely devoid of any disclosure with respect to the "bacterial RNAP homologous secondary channel amino acid sequence" and the mutant disclosed in Delgado and cited involves residue 931 of the β' subunit of RNAP from *E. coli*. Residue 931 is not part of, or even near to, a target region corresponding to, and alignable with residues 736-747 and 779-781 of the β' subunit of RNAP from *E. coli*. Furthermore, Applicant argues that at the time of the invention, there was no published disclosure, indeed not even published speculation, that MccJ25 functions through binding to the bacterial RNAP secondary channel specifically set forth in the claims.

9. Applicant's arguments have been considered but have not been found persuasive because Delgado et al disclose the β' subunit of *E. coli* RNAP, and the mutation in this strain was cloned by in vivo recombination into an rpoC+ plasmid. The presence of the recombinant plasmid conferred complete resistance to otherwise sensitive strains. Delgado et al further disclose that these results, along with the observation that MccJ25 inhibits in vivo and in vitro RNA synthesis, provide convincing evidence that RNAP is the target for MccJ25 action (see p. 4543, right column, 1st paragraph). Furthermore, the reference discloses that the putative target site for MccJ25 lies within a region spanning amino acids 842 to 1140 (thus containing segment

G), which has been shown to be exposed on the surface of RNAP (see p. 4549, left column, 1st paragraph). Applicant is reminded that the amendment to the claims comprises an "wherein clause", which does not carry a patentably weight. The claims are drawn to a method of identifying an agent that binds to a bacterial RNAP homologous secondary channel amino acid, and the residues are in the β' subunit of RNAP of *E. coli*. Since the primary reference teaches the β' subunit of RNAP of *E. coli*, an agent that binds to the β' subunit of RNAP of *E. coli* would necessarily bind to any amino acid residue of β' subunit of RNAP of *E. coli*. Furthermore, Korzheva et al teach that the secondary channel is responsible for the diffusion of incoming nucleotide substrate into the active site of RNAP (see abstract and Figure 3), to overcome access to the main channel which is blocked by the nucleic acid framework. Therefore, the rejection under 35 U.S.C. 103(a) is maintained.

10. With respect to claims 90, 92, 101 and 103, Delgado et al teachings are as discussed above. Further, Delgado disclose that the same comparative methods to detect activity in mutant bacterial RNAP can be applied to eukaryotes. The use of these methods resulted in locating the position of the mutant in yeast (eukaryote). This mutant as disclosed corresponds exactly to the above-mentioned mutant in bacterial RNAP that confers resistance to the antibiotic MccJ25. The difference between the reference and the instant claims is that the reference does not explicitly recite a derivative of human RNA polymerase.

11. However, Darst et al disclose methods of identifying an agent for use as inhibitors of eukaryotic RNAP polymerase (see claim 11). Further, Darst et al disclose that not all residues in the b' subunit of prokaryotic RNAP are conserved in eukaryotic RNA, pointing to the variable roles of the residues with respect to assembly and/or catalysis within the same subunit (see paragraphs [0176] and [0179]).

12. Woychik et al disclose that human and yeast RNAP II share a much higher level of sequence identity at both the surface and core positions (page 457, paragraph 3). However, there is no significant conservation of surface residues between yeast RNAP II and bacterial RNAP (page 457, paragraph 4).

13. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to use the method of identifying an agent that binds to a specific domain of prokaryotic RNAP with eukaryotic RNAP (human or yeast) for the known an expected result of providing a means recognized in the art to identify the basis of differential specificity within species and how that specificity contributes to sensitivity towards agents capable of inhibiting RNA synthesis activity. Furthermore, it would have been obvious to one or ordinary skill in the art at the time of invention to use the method of identifying an agent that binds to the bacterial RNAP secondary channel wherein agents other than MccJ25 are tested against MccJ25 as a control for the known and expected result of providing a means recognized in the art to compare the binding and inhibition properties of agents against a reference antibiotic known in the art to inhibit RNA synthesis by binding to RNAP.

Response to Applicant's Arguments

14. Applicant argues that the present invention provides the target region of the b' subunit of RNAP from E. coli, and corresponding residues of the b' subunit of RNAP from other bacterial species are also within the scope of the claims. Further, Applicant argues that at the time of the invention, there was no published disclosure, not even published speculation, that MccJ25 functions through binding to the bacterial RNAP secondary channel specifically set forth in the claims. There would be no basis to use a method of identifying an agent that binds to the target region specifically set forth in the claims wherein agents are tested against MccJ25 as control.

15. Applicant's arguments have been considered but have not been found persuasive because, as described supra, Delgado et al disclose the β' subunit of *E. coli* RNAP, and the mutation in this strain was cloned by in vivo recombination into an rpoC+ plasmid. The presence of the recombinant plasmid conferred complete resistance to otherwise sensitive strains. Delgado et al further disclose that these results, along with the observation that MccJ25 inhibits in vivo and in vitro RNA synthesis, provide convincing evidence that RNAP is the target for MccJ25 action (see p. 4543, right column, 1st paragraph). Furthermore, the reference discloses that the putative target site for MccJ25 lies within a region spanning amino acids 842 to 1140 (thus containing segment G), which has been shown to be exposed on the surface of RNAP (see p. 4549, left column, 1st paragraph). Applicant is reminded that the amendment to the claims comprises an "wherein clause", which does not carry a patentably weight. The

claims are drawn to a method of identifying an agent that binds to a bacterial RNAP homologous secondary channel amino acid, and the residues are in the β' subunit of RNAP of *E. coli*. Since the primary reference teaches the β' subunit of RNAP of *E. coli*, an agent that binds to the β' subunit of RNAP of *E. coli* would necessarily bind to any amino acid residue of β' subunit of RNAP of *E. coli*. Furthermore, Darst et al disclose methods of identifying an agent for use as inhibitors of eukaryotic RNAP, and that not all residues in the β' subunit of prokaryotic RNAP are conserved in eukaryotic RNA; Woychik et al disclose that human and yeast RNAP II share a much higher level of sequence identity at both the surface and core positions. However, there is no significant conservation of surface residues between yeast RNAP II and bacterial RNAP. Since human and yeast share a much higher level of sequence identity, and Darst et al disclose the methods of identifying an agent for use as inhibitors of eukaryotic RNAP, it would have been obvious to one of ordinary skill in the art to try human RNAP species to identify if the agents would work as inhibitors on human RNAP as well as eukaryotic (yeast) RNAP. Furthermore, it has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727,_;82 USPQ2d 1385, 1397

(2007). The "problem" facing those in the art was trying to understand the mechanism of action of MccJ25 (peptide antibiotic) and there were a limited number of methodologies available to do so, for example identifying the mutation causing resistance to MccJ25, and trying to identify the mutants affected in the target of the antibiotics. As described supra, Delgado teaches that MccJ25 RNA synthesis both in vivo and in vitro, and these results point to the RNA polymerase as the target of microcin action (see abstract, and p. 4543, right column, 1st paragraph). The skilled artisan would have had reason to try locating the sites of microcin action of the RNAP and comparing the MccJ25 mutants to MccJ25 wild-type, with the reasonable expectation that at least one would be successful. Delgado et al disclose β' subunit of the RNAP from *E. coli*, and the agent that binds to the subunit would bind to RNAP. Further, Darst et al disclose that not all residues in the b' subunit of prokaryotic RNAP are conserved in the eukaryotic RNA, and Woychik et al disclose that yeast RNAP II share a much higher level of sequence identity at both the surface and core positions with human RNAP, it would have been obvious to try examining those residues both within the surface and core positions and outside the surface and core positions of the sequences. Thus, examining other putative target sites outside the region and comparing the binding to MccJ25 as a control is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

*** Please note that this rejection below is further modified to address the rejection that was not addressed in the previous office action***

35 U.S.C. 112, 1st

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 86-89, 95 and 97-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

18. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

19. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

20. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court

determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

21. In the instant case, the claims are drawn to a method for identifying an agent that binds to a bacterial RNAP homologous secondary channel amino acid sequence in a first entity, wherein the first entity is selected from the group consisting of a derivative of *E. coli* RNAP and a derivative of *B. subtilis* RNAP, wherein the derivatives contain a bacterial RNAP homologus secondary channel amino acid sequence having at least one substitution, insertion, or deletion of amino acid residues corresponding to, an alignable with, amino acid residues 736-747 and 779-781 of the β' subunit of *E. coli* RNAP or amino acid residues 740-751 and 783-785 of the β' subunit of *B. subtilis* RNAP, respectively. The generic statements derivatives of *E. coli* and RNAP and *B. subtilis* RNAP, and secondary channel amino acid sequence having at least one substitution, insertion, or deletion of amino acid residues do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

22. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 85 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of amino acids or amino acid mimetics that can be substituted or inserted, and make up the class of sequences and derivatives of *E. coli* and RNAP and *B. subtilis* RNAP. It

must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives and variants. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules and other synthetic peptide or peptide-like molecule that can function as amino acids and amino acid like substituents.

23. The specification is limited to the amino acid substitutions at positions 424, 428, 429, 430, 454, 469, 493, 498, 503, 504, 508, 680, 684, 732, 733, 734, 735, 736, 738, 744, 748, 775, 776, 777, 778, 779, 780, 782, 783, 784, 785, 786, 788, 789, 790, 869, 922, 926, 927, 930, 931, 932, 933, 1136, 1137, 1240, 1241, 1244, 1247 and 1248. The working example describes that random mutagenesis was performed by error-prone PCR amplification, and the mutagenesis procedure yields all possible transition and transversion substitutions (see paragraph [0142]). The specification does not describe any deletion or insertion of amino acid residues. Description of single amino acid

substitution at positions 424, 428, 429, 430, 454, 469, 493, 498, 503, 504, 508, 680, 684, 732, 733, 734, 735, 736, 738, 744, 748, 775, 776, 777, 778, 779, 780, 782, 783, 784, 785, 786, 788, 789, 790, 869, 922, 926, 927, 930, 931, 932, 933, 1136, 1137, 1240, 1241, 1244, 1247 and 1248 is not sufficient to encompass numerous other peptide sequences that belong to the same genus. For example, the claims are drawn to amino acid sequence having at least one substitution, insertion, or deletion of amino acid residues corresponding to, and alignable with, amino acid residues 736-747 and 779-781 (β' subunit of *E. coli*) and 740-751 and 783-785 (β' subunit of *B. subtilis*). This implies that there are 12 different amino acid positions and 3 different amino acid positions for substitutions, insertion, or deletion for both subunits of the species. That means that there are at least 12*20=240 and 3*20 =60, respectively, different possibilities of substitutions, deletions and insertions. Furthermore, there are non-natural amino acids such as D-amino acids, α-amino acids, β-amino acids and ε-amino acids, that would further increase the number of substitution, insertion and deletions of amino acid residues. Having at least one insertion would increase the numbers of possibilities even further. There are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. For example, the specification only describes single amino acid substitutions of 736, 738, 744, 779 and 780 (E. coli) and 744, 748, 783, 784 and 785. However, there are no examples of deletions and insertions. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

24. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

25. In the previous office action, the rejection cited that to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlating, methods of making the claimed product, or any combination thereof. In this case, claims 86, 89, 95 and 99 are directed to identifying an agent that binds to RNAP secondary channel and derivatives of RNAP secondary channel having at least one substitution, insertion or deletion. Further, the claims are drawn to methods of identifying an agent that binds to derivative of an eukaryotic RNAP derivative when compared with an agent that binds to a bacterial RNAP secondary channel. While the specification has adequate written description of the RNAP secondary channel, there is no disclosure on the structural limitations of the genus represented by the derivatives of RNAP secondary channel and the genus

represented by eukaryotic RNAP. Further, there is no disclosure of the activity of the above-mentioned derivatives, nor any method to analyze the activity of the derivatives. There is no description of the identifying characteristics for recognizing that an agent will inhibit the activity of the derivative of RNAP. One skilled in the art would conclude that the disclosure of intact RNAP secondary channel or eukaryotic RNAP is not representative of the undefined genus of derivatives recited in the claims. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Therefore, the inventor, at the time the application was filed was not in possession of the broad genus comprising "derivatives of bacterial RNAP secondary channel" and "derivatives of eukaryotic RNAP" needed to practice the claimed invention.

Response to Applicant's Arguments

26. Applicant argues that with respect to derivatives of eukaryotic RNAP, Applicants have amended the claims to remove the "derivative" language and to recite human RNAP I, human RNAP II, and human RNAP III, and these structures are well known in the art and FIG 1 shows a partial amino acid sequence of human RNAP I, II and III relevant to the instant application.

27. Applicant's arguments have been considered, and Applicant's amendments to the claims are acknowledged in regards to the "derivatives of eukaryotic RNAP". However, since the rejection has been further modified to include the issues that were

never addressed in the previous office action, revised rejection under 35 U.S.C. 112, first paragraph is described above, and therefore, Applicant's arguments have not been found persuasive.

New Rejections

35 U.S.C. 112, 2nd

28. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

29. Claim 86, recites the limitation "amino acid residues 740-751 and 783-785 of the β' subunit of *Bacillus subtilis* RNAP" in 6th and 7th line of the claim. There is insufficient antecedent basis for this limitation in the claim. The base claim 84 only recites that the bacterial RNAP homologous secondary channel amino acid sequence corresponds to, and is alignable with, amino acid residues 736-747 and 779-781 of the β' subunit of RNAP from *E. coli*. The base claims does not recite β' subunit of *Bacillus subtilis* RNAP, therefore, claim 86 lacks antecedent basis.

30. Claim 89 recites the limitation " a derivative of *Bacillus subtilis* RNAP" in 2nd and 3rd line of the claim and "amino acid residues 740-751 and 783-785 of the β' subunit of *Bacillus subtilis* RNAP" in 6th and 7th line of the claim. There is insufficient antecedent basis for this limitation in the claim. The base claim 84 only recites that the bacterial RNAP homologous secondary channel amino acid sequence corresponds to, and is alignable with, amino acid residues 736-747 and 779-781 of the β' subunit of RNAP from *E. coli*. Furthermore, claim 87, which claim 89 is dependent from, only recites the

β' subunit of RNAP from *E. coli*. The base claims does not recite β' subunit of *Bacillus subtilis* RNAP, therefore, claim 89 lacks antecedent basis.

31. Claim 95 recites the limitation " a derivative of *Bacillus subtilis* RNAP" in 2nd and 3rd line of the claim and "amino acid residues 740-751 and 783-785 of the β' subunit of *Bacillus subtilis* RNAP" in 6th and 7th line of the claim. There is insufficient antecedent basis for this limitation in the claim. The base claim 84 only recites that the bacterial RNAP homologous secondary channel amino acid sequence corresponds to, and is alignable with, amino acid residues 736-747 and 779-781 of the β' subunit of RNAP from *E. coli*. Furthermore, claim 93, which claim 95 is dependent from, only recites the β' subunit of RNAP from *E. coli*. The base claims does not recite β' subunit of *Bacillus subtilis* RNAP, therefore, claim 95 lacks antecedent basis.

32. Claim 99 recites the limitation " a derivative of *Bacillus subtilis* RNAP" in 2nd and 3rd line of the claim and "amino acid residues 740-751 and 783-785 of the β' subunit of *Bacillus subtilis* RNAP" in 6th and 7th line of the claim. There is insufficient antecedent basis for this limitation in the claim. The base claim 84 only recites that the bacterial RNAP homologous secondary channel amino acid sequence corresponds to, and is alignable with, amino acid residues 736-747 and 779-781 of the β' subunit of RNAP from *E. coli*. Furthermore, claim 97, which claim 99 is dependent from, only recites the β' subunit of RNAP from *E. coli*. The base claims does not recite β' subunit of *Bacillus subtilis* RNAP, therefore, claim 95 lacks antecedent basis.

33. Claims 86, 89, 95 and 99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. The claims recite "derivatives of *E. coli* and RNAP and *B. subtilis* RNAP". It is unclear what type of modifications and changes would constitute derivatives of *E. coli* and RNAP and *B. subtilis* RNAP. For example, there are physical, enzymatic or chemical changes that can affect changes in the structure of compounds that may constitute a derivative of *E. coli* and RNAP and *B. subtilis* RNAP.

Obviousness Double Patenting

34. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

35. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

36. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

37. Claims 84-90, 92-101 and 103 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-12 and 17-25 of copending Application No. 10/571226. Although the conflicting claims are not identical, they are not patentably distinct from each other because if one of ordinary skill in the art practiced the claimed invention of copending application, one would necessarily arrive at the instant claimed invention.

38. Claims 84-90, 92-101 and 103 of instant application are drawn to a method for identifying an agent that binds to a bacterial RNAP homologous secondary channel amino acid sequence in a first entity, comprising the steps of: (a) preparing a reaction solution including the agent to be tested and a first entity including a bacterial RNAP homologous secondary chancel amino acid sequence; and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the bacterial RNAP homologous secondary channel amino acid sequence; wherein said bacterial RNAP homologous secondary channel amino acid sequence corresponds to, and is alignable with, amino acid residues 736-747 and 779-781 of the β' subunit of RNAP from *E. coli*. Furthermore, the claims are drawn to the first entity selected from the group consisting of an intact bacterial RNAP and a fragment of a bacterial RNAP, wherein the first entity is selected from a group consisting of a derivative of *E. coli* RNAP and a derivative of *B. subtilis* RNAP (see claims 84-89). Further, the claims are drawn to comprising comparison of (a) at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the first entity; and (b) at least one of the presence, extent, concentration-dependence, or kinetics of binding of

the agent to a human RNAP selected from the group consisting of human RNAP I, human RNAP II, and human RNAP III, and the presence, extent, concentration-dependence, or kinetics of inhibitions by MccJ25 of an activity of the first entity (see claims 90, 92-101 and103).

39. Claims 8-12 and 17-25 of the co-pending application are drawn to a method for identifying an agent that binds to a bacterial RNAP homologous secondary channel amino acid sequence, comprising (a) preparing a reaction solution comprising the agent to be tested, a reference compound according to claim 1, and a first entity containing a bacterial RNAP homologous secondary channel amino acid sequence, and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of competition b the agent for binding of the reference compound to the homologous secondary channel amino acid sequence, wherein the first entity is an intact bacterial RNAP or a fragment of a bacterial RNAP and is a derivative of *E. coli* RNAP or *B. subtilis* RNAP (see claims 8-12). Furthermore, the claims are drawn to a method further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of the binding of the agent to the first entity; and (b) at least one of the presence, extent, concentration-dependence, or kinetics of the binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous secondary channel amino acid sequence having at least one substitution, insertion or deletion, and the presence, extent, concentration-dependence, or kinetics of binding of MccJ25 to the fist entity (see claims 17-25).

40. If one of ordinary skill in the art practiced the claimed invention of instant application, one would necessarily arrive at the claimed invention of co-pending application 10/571226 and vice versa.

41. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

42. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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10/12/07
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